```
=> s (interleukin()13) and receptor

L1        1064 (INTERLEUKIN(W) 13) AND RECEPTOR

=> s l1 and py<1996

   2 FILES SEARCHED...
L2         215 L1 AND PY<1996

=> s l2 and ((IL()13Rb) or (IL()13rbeta))

L3           0 L2 AND ((IL(W) 13RB) OR (IL(W) 13RBETA))

=> s (interleukin()13) adj receptor

MISSING OPERATOR 13) ADJ
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s interleukin()13 () receptor

L4         257 INTERLEUKIN(W) 13 (W) RECEPTOR

=> s l4 and py<1996
<------User Break------>
u
SEARCH ENDED BY USER

=> s l4 and py<1996

   2 FILES SEARCHED...
L5          33 L4 AND PY<1996

=> dup rem l5

PROCESSING COMPLETED FOR L5
L6           21 DUP REM L5 (12 DUPLICATES REMOVED)

=> d l6 ibib abs tot


L6   ANSWER 1 OF 21  MEDLINE
ACCESSION NUMBER:    95348103     MEDLINE
DOCUMENT NUMBER:     95348103
TITLE:               A novel chimeric protein composed of interleukin 13 and
                     Pseudomonas exotoxin is highly cytotoxic to human
carcinoma
                     cells expressing receptors for interleukin 13 and
                     interleukin 4.
AUTHOR:              Debinski W; Obiri N I; Pastan I; Puri R K
CORPORATE SOURCE:    Milton S. Hershey Medical Center, Department of Surgery,
                     Pennsylvania State University, Hershey 17033, USA.
SOURCE:              JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Jul 14)
                     270 (28) 16775-80.
                     Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals; Cancer Journals
ENTRY MONTH:         199511
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AB Chimeric proteins provide a unique opportunity to target therapeutic bacterial toxins to a subset of specific cells. We have generated a new recombinant chimeric toxin composed of human interleukin 13 (hIL13) and a Pseudomonas exotoxin A (PE) mutant, PE38QQR. The hIL13-PE38QQR chimera is highly cytotoxic to cell lines derived from several human epithelial carcinomas such as adenocarcinoma of stomach, colon, and skin. The cytotoxic action of hIL13-PE38QQR, which can only occur upon internalization of ligand-receptor complex, is blocked by an excess of hIL13 but not of hIL2. This action is not solely hIL13-specific because an excess of hIL4 also blocks the cytotoxicity of hIL13-toxin. Conversely, hIL13 blocks the cytotoxicity of a hIL4-PE38QQR chimera. Binding studies showed that hIL13 displaces competitively 125I-labeled hIL4-PE38QQR on carcinoma cells. These results indicate that IL4 and IL13 compete for a common binding site on the studied human cell lines. Despite this competition, hIL4 but not hIL13 decreased protein synthesis in malignant cells susceptible to the cytotoxicity of both hIL13- and hIL4-PE38QQR. Our results suggest that a spectrum of human carcinomas express binding sites for IL13. Furthermore, hIL13 and hIL4 compete reciprocally for a form of the receptor that is internalized upon binding a ligand. Thus, cancer cells represent an interesting model for studying receptors for these two growth factors. Finally, hIL13-PE38QQR may be a useful agent in the treatment of several malignancies.

L6 ANSWER 2 OF 21 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95293986 MEDLINE
DOCUMENT NUMBER: 95293986
TITLE: The primary binding subunit of the human interleukin-4 receptor is also a component of the **interleukin-13 receptor.**
AUTHOR: Zurawski S M; Chomarat P; Djossou O; Bidaud C; McKenzie A N; Miossec P; Banchereau J; Zurawski G
CORPORATE SOURCE: Department of Molecular Biology, DNAX Research Institute of Cellular and Molecular Biology, Palo Alto, California 94304-1104, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1995 Jun 9)** 270 (23) 13869-78.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199509
AB Interleukin (IL)-13 elicits a subset of the biological activities of the related IL-4. The basis of this functional similarity is that their specific cell-surface receptors (called IL-13R and IL-4R) are distinct, yet are complex and share a common subunit(s). The IL-4R primary binding subunit (called IL-4R alpha) does not by itself bind IL-13. We show that the ability of IL-13 to partially compete for IL-4 binding to some human cell types depended on co-expression of IL-4R and IL-13R. However, IL-13 binding was always associated with IL-4 binding. Hyper-expression of IL-4R alpha on cells expressing both IL-4R and IL-13R decreased their binding affinity for IL-4, abrogated the ability of IL-13 to compete for IL-4 binding, and yet had no effect on IL-13R properties. Anti-human IL-4R alpha monoclonal antibodies which blocked the biological function and binding of IL-4 also blocked the function and binding of IL-13. These data show that IL-4R alpha is a secondary component of IL-13R.

L6 ANSWER 3 OF 21 MEDLINE
ACCESSION NUMBER: 95263584 MEDLINE
DOCUMENT NUMBER: 95263584
TITLE: Interleukin-13 signal transduction in lymphohemopoietic

cells. Similarities and differences in signal transduction with interleukin-4 and insulin.

AUTHOR: Wel[redacted]m M J; Learmonth L; Bone H; Sch[redacted]der J W

CORPORATE SOURCE: Biomedical Research Centre, University of British Columbia, Vancouver, Canada.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1995 May 19)** 270 (20) 12286-96.
Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199508

AB Interleukin-13 (IL-13) and interleukin-4 (IL-4) are related in structure and function and are thought to share a common receptor component. We have investigated the signal transduction pathways activated by these two growth factors, as well as insulin, in cell-lines and primary cells of lymphohemopoietic origin. All three factors induced the tyrosine phosphorylation of a protein of 170 kDa (p170), which coimmunoprecipitated with the p85 subunit of P13'-kinase, via high affinity interactions mediated by the SH2 domains of p85. Antibodies raised against the entire insulin-receptor substrate-1 (IRS-1) protein immunoprecipitated p170 much less efficiently than they did IRS-1 from 3T3 cells. However, antibodies directed against the conserved pleckstrin homology domain of IRS-1 immunoprecipitated both p170 and IRS-1 with similar efficiency, suggesting they share structural similarities in this region. In lymphohemopoietic cells, IL-13, IL-4, and insulin failed to induce increased tyrosine phosphorylation of Shc, or its association with grb2, modification of Sos1, or activation of erk-1 and erk-2 mitogen-activated protein kinases, suggesting that p170 mediates downstream pathways distinct from those mediated by IRS-1. Both IL-13 and IL-4 induced low levels of tyrosine phosphorylation of Tyk-2 and Jak-1. IL-4 also activated the Jak-3-kinase, but, despite other similarities, IL-13 did not. Insulin failed to activate any of the known members of the Janus family of kinases. In that Jak-3 is reported to associate with the IL-2 gamma c chain, these data suggest that the IL-13 receptor does not utilize this subunit. However, both IL-13 and IL-4 induced tyrosine phosphorylation of the IL-4-140 kDa receptor chain, suggesting that this is a component of both receptors in these cells and accounts for the similarities in signaling pathways shared by IL-13 and IL-4.

L6 ANSWER 4 OF 21 MEDLINE

ACCESSION NUMBER: 95238374 MEDLINE

DOCUMENT NUMBER: 95238374

TITLE: Receptor for interleukin 13. Interaction with interleukin 4 by a mechanism that does not involve the common gamma chain shared by receptors for interleukins 2, 4, 7, 9, and 15.

AUTHOR: Obiri N I; Debinski W; Leonard W J; Puri R K

CORPORATE SOURCE: Laboratory of Molecular Tumor Biology, Food and Drug Administration, Bethesda, Maryland 20892, USA.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1995 Apr 14)** 270 (15) 8797-804.
Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199507

AB Interleukin 13 (IL-13) shares many biological properties with IL-4, and although the receptor for IL-4 (IL-4R) has been characterized, the expression and structure of IL-13 receptor are unknown. We report here that human renal cell carcinoma (RCC) cells express large numbers of functional IL-13R. Human B lymphocytes and monocytes expressed a very small number of IL-13R, while resting or activated human T cells expressed little or no IL-13R. IL-4 did not compete for IL-13 binding, while IL-13 competed for IL-4 binding, even though IL-4R and IL-13R are structurally distinct on human RCC cells. IL-13 cross-linked with one major protein that is similar in size to the gamma c subunit of IL-2, -4, -7, -9, and -15 receptors but was not recognized by anti-gamma c or anti-IL-4R antibodies. IL-4, on the other hand, cross-linked with two major proteins, the smaller of which appears to be similar in size to IL-13R and gamma c, but (like the IL-13R) it did not react with anti-gamma c antibody. Although as shown in this study and in previous studies, gamma c is a functional component of IL-4R in lymphoid cells, it does not appear to be associated with IL-4R on RCC cells. Even in the absence of common gamma chain IL-4 and IL-13 were able to up-regulate intracellular adhesion molecule-1 antigen on RCC cells. These data suggest that the interaction of IL-13 with IL-4R does not involve gamma c and IL-13R itself may be a novel subunit of the IL-4R.

L6 ANSWER 5 OF 21 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 96025882 MEDLINE
DOCUMENT NUMBER: 96025882
TITLE: IL-4 induces germ-line IgE heavy chain gene transcription in human fetal pre-B cells. Evidence for differential expression of functional IL-4 and IL-13 receptors during B cell ontogeny.
AUTHOR: Punnonen J; Cocks B G; de Vries J E
CORPORATE SOURCE: DNAX Research Institute of Molecular and Cellular Biology, Human Immunology Department, Palo Alto, CA 94304, USA.
SOURCE: JOURNAL OF IMMUNOLOGY, **(1995 Nov 1)** 155 (9) 4248-54.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199602
AB The present study demonstrates that IL-4 induces germ-line IgE heavy chain (epsilon) gene transcription in human fetal splenic mononuclear cells; fetal bone marrow cells; highly purified sorted surface (s) mu+, CD10+, CD19+ immature B cells; and s mu-, cytoplasmic mu+, CD10+, CD19+ pre-B cells derived from human fetal bone marrow. Similar to observations in normal adult B cells, TGF-beta and IFN-gamma inhibited IL-4-induced germ-line epsilon RNA synthesis in fetal pre-B cells, whereas anti-CD40 mAbs and TNF-alpha had enhancing effects, suggesting that the general mechanisms regulating germ-line epsilon transcription in adult B cells and pre-B cells are similar. IL-13 also induced germ-line epsilon RNA synthesis in s mu+, CD10+, CD19+ immature B cells, but the level of transcription induced by IL-13 was significantly less than that induced by IL-4. Anti-CD40 mAbs strongly synergized with both IL-4 and IL-13 in inducing germ-line epsilon RNA synthesis by fetal immature B cells. Interestingly, IL-13 failed to induce germ-line epsilon RNA synthesis in s mu- pre-B cells even in the presence of anti-CD40 mAbs. These distinct effects of IL-4 and IL-13 suggest that functional IL-13R are expressed at a later stage of B cell ontogeny than IL-4R, and that IL-13, in contrast to IL-4, does not regulate pre-B cell differentiation. Given the fact that

IL-4 production appears to be enhanced in atopic individuals, the capacity of IL-4 to induce germ-line epsilon transcription in human fetal immature B cells and pre-B cells suggests that commitment of B cell precursors to IgE-producing cells may occur during intrauterine life and may explain the increased IgE production in neonates with a family history of atopy.

L6 ANSWER 6 OF 21 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 96025871 MEDLINE
DOCUMENT NUMBER: 96025871
TITLE: IL-4 induces human B cell maturation and IgE synthesis in SCID-hu mice. Inhibition of ongoing IgE production by in vivo treatment with an IL-4/IL-13 receptor antagonist.
AUTHOR: Carballido J M; Schols D; Namikawa R; Zurawski S; Zurawski G; Roncarolo M G; de Vries J E
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute, Palo Alto, CA 94304, USA.
SOURCE: JOURNAL OF IMMUNOLOGY, **(1995 Nov 1)** 155 (9) 4162-70.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199602
AB The effect of cytokine treatment on the in vivo maturation and Ig isotype switching of human B cells was studied in a modified SCID-hu mouse model. SCID mice, subcutaneously cotransplanted with small fragments of fetal human thymus and bone (SCID-hu BM/T mice) generated all human leukocyte lineages including T and B lymphocytes, macrophages, and granulocytes. All SCID-hu BM/T mice spontaneously produced human IgM and IgG, whereas IgE and IgA were detected in 37 and 80% of the mice, respectively, indicating that productive human T-B cell interactions resulting in Ig isotype switching occur in these mice. Administration of IL-4 to SCID-hu BM/T mice enhanced human B cell maturation, as judged by the increase in the percentages of CD45+, CD19+ bone marrow B cells expressing CD20, CD23, CD40, sIgM, and sIgD. Furthermore, these cells were also functionally more mature because they spontaneously produced human IgG/IgG4 in vitro and could be induced to secrete human IgE by addition of anti-CD40 mAb alone. In contrast, B cells isolated from PBS-treated mice only produced significant Ig levels after stimulation with anti-CD40 mAb in the presence of exogenous IL-4. IL-4 administration also induced human IgE synthesis in 44% of the mice, which had no serum IgE before treatment. More importantly, ongoing human IgE synthesis in SCID-hu BM/T mice was suppressed by > 90% following administration of an IL-4 mutant protein, which acts as an IL-4 and IL-13 receptor antagonist. These results suggest that IL-4/IL-13 receptor antagonists have potential clinical utility in treating human atopic diseases associated with enhanced IgE production.

L6 ANSWER 7 OF 21 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 95181299 MEDLINE
DOCUMENT NUMBER: 95181299
TITLE: Characterization and comparison of the **interleukin 13 receptor** with the interleukin 4 receptor on several cell types.
AUTHOR: Vita N; Lefort S; Laurent P; Caput D; Ferrara P
CORPORATE SOURCE: Sanofi Recherche, Lab`ege, France.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1995 Feb 24)**

270 (8) 3512-7.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199506
AB We describe here the characterization of the interleukin (IL) 13 receptor and a comparison with the IL-4 receptor on different cell types. Several, but not all, of the IL-4 receptor-positive cells showed specific IL-13 binding, which was always completely displaced by IL-4. In the IL-13 receptor-positive cells, the IL-13 either completely or partially displaced the labeled IL-4. Further characterization of the IL-13 receptor in two cell lines, COS-3 and A431, representative of the groups of complete and partial displacement of IL-4 by IL-13, respectively, showed that the IL-13 binds with high affinity (Kd approximately 300 pM) to both cells and that the number of binding sites is, in COS-3 cells, equivalent to that for IL-4 and, in A431 cells, is smaller than that for IL-4. Cross-linking of labeled IL-13 yielded, on COS-3 cells, two affinity-labeled complexes of 220 and 70 kDa, and on A431 cells, one complex of 70 kDa; labeled IL-4 yielded on both cells the same pattern of three complexes of 220, 145, and 70 kDa. Altogether, these results suggest that the IL-13 receptor may be constituted by a subset of the IL-4 receptor complex associated with at least one additional protein.

L6 ANSWER 8 OF 21 MEDLINE
ACCESSION NUMBER: 96091795 MEDLINE
DOCUMENT NUMBER: 96091795
TITLE: Differential regulation of IL-13 and IL-4 production by human CD8+ and CD4+ Th0, Th1 and Th2 T cell clones and EBV-transformed B cells.
AUTHOR: de Waal Malefyt R; Abrams J S; Zurawski S M; Lecron J C; Mohan-Peterson S; Sanjanwala B; Bennett B; Silver J; de Vries J E; Yssel H
CORPORATE SOURCE: Department of Human Immunology, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104, USA.
SOURCE: INTERNATIONAL IMMUNOLOGY, **(1995 Sep)** 7 (9) 1405-16.
Journal code: AY5. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
AB In the present study, the requirements and characteristics for the production of IL-13 by human T cells, T cell clones and B cells were determined and compared with those of IL-4. IL-13 was produced by human CD4+ and CD8+ T lymphocyte subsets isolated from peripheral blood mononuclear cells and by CD4+ and CD8+ T cell clones. CD4+ T cell clones belonging to Th0, Th1-like and Th2-like subsets produced IL-13 following antigen-specific or polyclonal activation. In addition, EBV-transformed B cell lines expressed IL-13 mRNA and produced small amounts of IL-13 protein. Expression of IL-13 mRNA and production of IL-13 protein by peripheral blood T cells and T cell clones was induced rapidly and was relatively long lasting, whereas IL-4 production by these cells was transient. In addition, IL-13 mRNA expression was induced by modes of activation that failed to induce IL-4 mRNA expression. IL-13 shares many biological activities with IL-4 which is compatible with the notion that the IL-13 and IL-4 receptors share a common component required for signal transduction. However, IL-13 lacks the T cell-activating properties of IL-4. Here we have shown that this is related to the fact that T cells fail to bind radiolabeled IL-13 and do not express the IL-13-specific receptor component. Taken together, these results indicate that the

differences in expression and biological activities of IL-4 and IL-13 on T cells may have consequences for the relative roles of these cytokines in the immune response.

L6 ANSWER 9 OF 21 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999034937 MEDLINE
DOCUMENT NUMBER: 99034937
TITLE: Human glioma cells overexpress receptors for interleukin 13 and are extremely sensitive to a novel chimeric protein composed of interleukin 13 and pseudomonas exotoxin.
AUTHOR: Debinski W; Obiri N I; Powers S K; Pastan I; Puri R K
CORPORATE SOURCE: The Milton S. Hershey Medical Center, The Pennsylvania State University College of Medicine, Department of Surgery, Division of Neurosurgery, Hershey, Pennsylvania 17033, USA.. debinski@debin.nsr.hmc.psu.edu
SOURCE: CLINICAL CANCER RESEARCH, **(1995 Nov)** 1 (11) 1253-8.
Journal code: C2H. ISSN: 1078-0432.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY WEEK: 19990402
AB Recently, we have demonstrated that a spectrum of human adenocarcinoma cell lines express binding sites for interleukin 13 (IL-13). These cells are killed by a chimeric protein composed of human (h) IL-13 and a derivative of Pseudomonas exotoxin, PE38QQR (Debinski et al., J. Biol. Chem., 270: 16775-16780, 1995). The cell killing was hIL-13- and hIL-4-specific, indicating that a common binding site for the two cytokines is present in several solid tumor cell lines. Herein, we report that an array of established glioma cell lines is killed by very low concentrations of hIL-13-PE38QQR, often reaching <1 ng/ml (<20 pM). Glioma cells express up to 30,000 molecules of IL-13 receptor/cell which has intermediate affinity toward hIL-13. hIL-13-PE38QQR is more active (up to 3 logs difference in cytotoxic activities) than are the corresponding chimeric toxins containing hIL-4 or hIL-6. The cytotoxic action of hIL-13-PE38QQR is blocked by an excess of hIL-13 on all cell lines studied, and it is not neutralized by hIL-4 on some of these cells. Our results show that human brain cancers richly express receptors for IL-13. Furthermore, the interaction detected previously between receptors for IL-13 and IL-4 on solid tumors cell lines is of a qualitatively different character in U-251 MG and U-373 MG glioma cells. The receptor for IL-13 may represent a new marker of brain cancers and an attractive target for anticancer therapies.

L6 ANSWER 10 OF 21 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:197687 BIOSIS
DOCUMENT NUMBER: PREV199598211987
TITLE: Gamma-c subunit of the IL-2R does not function as the shared subunit for the IL-4R and IL-13R.
AUTHOR(S): He, Y.-W.; Malek, T. R.
CORPORATE SOURCE: Dep. Microbiol. Immunol., Univ. Miami Sch. Med., Miami, FL 33136 USA
SOURCE: FASEB Journal, (1995) Vol. 9, No. 4, pp. A1020.
Meeting Info.: Experimental Biology 95, Part II Atlanta, Georgia, USA April 9-13, 1995
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 11 OF 21 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96245780 MEDLINE

DOCUMENT NUMBER: 96245780
TITLE: Characterization of **interleukin-13 receptor** in carcinoma cell lines and human blood cells and comparison with the interleukin-4 receptor.
AUTHOR: Feng N; Schnyder B; Vonderschmitt D J; Ryffel B; Lutz R A
CORPORATE SOURCE: Institute of Clinical Chemistry, University Hospital Zurich.
SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, **(1995 Sep-Dec)** 15 (7-8) 931-49.
Journal code: CCU. ISSN: 1079-9893.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610

AB The **interleukin-13 receptor** is characterized by ligand-binding and crosslinking studies and compared with the interleukin-4 receptor. Crosslinking of radio-labeled hIL-4 and hIL-13 to the receptors on human carcinoma and mast cell lines demonstrated a predominant subunit at 130 kDa with two other minor bands of lower molecular mass (75 kDa and 65 kDa) in autoradiography. All binding of 125I-IL-13 was specifically blocked when the carcinoma cell suspensions were incubated with an excess of unlabeled hIL-4. However, unlabeled hIL-13 was unable to completely displace 125I-hIL-4 from the 130 kDa protein. In addition, 125I-hIL-13 showed no binding to mouse fibroblast cells transfected with human 130 kDa hIL-4 receptor c-DNA. Using weighted nonlinear computer modeling of the data from several equilibrium binding studies with human mast cells, a model of two binding sites for IL-4 (Kd = 50 and 190 pmol/L) and one site for IL-13 (Kd = 100 pmol/L) fitted better than a one site model with a very high level of significance (F = 10.66, P < 0.0001). It can be concluded that human IL-4R and hIL-13R are similar but distinct. This conclusion is supported here for the first time by a strong statistical criterion.

L6 ANSWER 12 OF 21 MEDLINE
ACCESSION NUMBER: 96418801 MEDLINE
DOCUMENT NUMBER: 96418801
TITLE: Interleukin-13: characterization and biologic properties.
AUTHOR: McKenzie A N; Zurawski G
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Cambridge, United Kingdom.
SOURCE: CANCER TREATMENT AND RESEARCH, **(1995)** 80 367-78.
Ref: 43
Journal code: AVA. ISSN: 0927-3042.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY WEEK: 19970204

L6 ANSWER 13 OF 21 MEDLINE
ACCESSION NUMBER: 96172542 MEDLINE
DOCUMENT NUMBER: 96172542
TITLE: Interleukin 13 suppresses cytokine production and stimulates the production of 15-HETE in PBMC. A comparison between IL-4 and IL-13.
AUTHOR: Deleuran B; Iversen L; Deleuran M; Yssel H; Kragballe K; Stengaard-Pedersen K; Thestrup-Pedersen K
CORPORATE SOURCE: Department of Rheumatology, University Hospital of Aarhus, Denmark.
SOURCE: CYTOKINE, **(1995 May)** 7 (4) 319-24.

Journal code: A52. ISSN: 1043-4666.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605

AB We examined the ability of rIL-13 to regulate rIL-1 alpha induced IL-1 beta, IL-1 receptor antagonist (IL-1ra) and IL-8 production in cultured peripheral blood mononuclear cells (PBMC), endothelial cells and fibroblasts. Furthermore we examined whether rIL-13 could influence the production of the arachidonic acid products LTB4, 12-HETE and 15-HETE by PBMC. rIL-1 alpha-stimulated PBMC cultures secreted high levels of IL-1 beta and IL-8; this could be inhibited to the level of unstimulated control cells by co-incubation with rIL-13 (10 ng/ml). IL-13 induced a 3-fold increase of the IL-1ra secretion which was inhibited by rIFN-gamma.

In the presence of both rIL-1 alpha and rIL-13, endothelial cells increased IL-8 secretion, whereas dermal fibroblasts remained unchanged. Of the arachidonic acid metabolites examined, the greatest change was observed in the formation of 15-HETE. In unstimulated PBMC cultures the amount of 15-HETE was less than 4 ng/10(6) cells, whereas after addition of rIL-13 we measured a formation of 139 +/- 6.2 ng/10(6) cells. The effect of rIL-13 on the 15-HETE formation in PBMC was abolished by addition of 100 U/ml rIFN-gamma. rIL-13 only induced minor changes in the LTB4 and 12-HETE formation. Compared to IL-4, IL-13 induced a similar alteration of the cytokine cascade and arachidonic acid metabolism, supporting the hypothesis that the two cytokines use a common receptor complex or signal pathway.

L6 ANSWER 14 OF 21 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 95337763 MEDLINE
DOCUMENT NUMBER: 95337763
TITLE: Inhibition of human IgE synthesis in vitro and in SCID-hu mice by an interleukin-4 receptor antagonist.
AUTHOR: Carballido J M; Aversa G; Schols D; Punnonen J; de Vries J E
CORPORATE SOURCE: Human Immunology Department, DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104, USA.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, **(1995 May-Jun)** 107 (1-3) 304-7.
Journal code: BJ7. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510

AB In the present study, it is shown that a human interleukin (IL)-4 mutant protein (IL-4.Y124D) acts as a potent IL-4 and IL-13 receptor antagonist. Human (h) IL-4.Y124D efficiently inhibits both IL-4- and IL-13-induced IgE production in vitro. In addition, hIL-4.Y124D strongly inhibits ongoing human IgE synthesis in SCID-hu mice. These inhibitory effects are specific, since human IgG levels were not significantly affected. These results confirm the notion that the IL-4 and IL-13 receptor share a common component, which is required for signal transduction. In addition, they show that relatively large antagonistic polypeptides, such as hIL-4.Y124D have potential clinical utility in reducing IgE-mediated allergic diseases.

L6 ANSWER 15 OF 21 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1996:45270 BIOSIS
DOCUMENT NUMBER: PREV199698617405
TITLE: Characterization of human **interleukin-13** -**receptor**: Evidence for a shared receptor subunit

with IL-4.
AUTHOR(S): Aman, M. J. (1); Lin, J.-X.; Zhou, L.; Weatherbee, J. A.; Ts[redacted], M.; Leonard, W.
CORPORATE SOURCE: (1) Lab. Mol. Immunol., Natl. Heart Lung Blood Inst., Bethesda, MD 20892 USA
SOURCE: Onkologie, (1995) Vol. 18, No. SUPPL. 2, pp. 124.
Meeting Info.: Annual Congress of the German and Austrian Societies for Hematology and Oncology Hamburg, Germany October 8-11, 1995
ISSN: 0378-584X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 16 OF 21 MEDLINE
ACCESSION NUMBER: 95309415 MEDLINE
DOCUMENT NUMBER: 95309415
TITLE: IL-13 and IL-4 share signal transduction elements as well as receptor components in TF-1 cells.
AUTHOR: Lefort S; Vita N; Reeb R; Caput D; Ferrara P
CORPORATE SOURCE: Sanofi Recherche, Lab`ege Innopole, France.
SOURCE: FEBS LETTERS, **(1995 Jun 12)** 366 (2-3) 122-6.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199509
AB IL-13 and IL-4 are growth factors for the human erythroleukemia cell line TF-1. In these cells both cytokines share overlapping binding sites, but the number of sites for IL-13 is half of that for IL-4. Two monoclonal antibodies against the extracellular domain of the IL-4R alpha chain completely abolish the binding of IL-13, although IL-13 does not bind to this chain. Following receptor triggering, IL-13 and IL-4 induce the phosphorylation of a 170 kDa protein, probably the IL-4-induced phosphotyrosine substrate. In addition the phosphorylation of the 170 kDa protein results in its tight association with phosphatidylinositol-3-kinase.

L6 ANSWER 17 OF 21 MEDLINE
ACCESSION NUMBER: 95325632 MEDLINE
DOCUMENT NUMBER: 95325632
TITLE: The IL-2 receptor gamma c chain does not function as a subunit shared by the IL-4 and IL-13 receptors.
Implication
for the structure of the IL-4 receptor.
AUTHOR: He Y W; Malek T R
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Miami School of Medicine, FL 33136, USA.
CONTRACT NUMBER: 1R01-CA45957 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGY, **(1995 Jul 1)** 155 (1) 9-12.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199510
AB The IL-2 receptor (IL-2R) gamma c subunit is also a component of the receptors for IL-4, IL-7, IL-9, and IL-15. The IL-4R and IL-13R appear to share a common subunit, and gamma c was proposed to be this shared subunit. In this study, we have assessed the relative contribution of gamma c to the mouse IL-4R and IL-13R. The MC/9 mast cell line constitutively expresses gamma c and proliferates to IL-4 and IL-13, but only the response to IL-4 was blocked by anti-gamma c mAbs. After transfection of the IL-4- and IL-13-responsive gamma c-negative B9 plasmacytoma with full length (m gamma) or cytoplasmic-tailless gamma c

cDNA (m gamma t), only the proliferative response to IL-4 was affected by the surface expression of these gamma c molecules. The inability of m gamma or m gamma [redacted] expression to affect IL-13-indu[redacted] proliferation by B9 indicates that gamma c does not obviously contribute to the IL-13R and does not function as the shared subunit of the IL-4R and IL-13R. This study suggests that there are two distinct IL-4R, one of which is independent of gamma c.

L6 ANSWER 18 OF 21 MEDLINE
ACCESSION NUMBER: 95002936 MEDLINE
DOCUMENT NUMBER: 95002936
TITLE: Interleukin-13 inhibits the proliferation of normal and leukemic human B-cell precursors.
AUTHOR: Renard N; Duvert V; Banchereau J; Saeland S
CORPORATE SOURCE: Schering-Plough, Laboratory for Immunological Research, Dardilly, France.
SOURCE: BLOOD, **(1994 Oct 1)** 84 (7) 2253-60.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199501
AB Interleukin-13 (IL-13) is a T-cell-derived cytokine that displays homology with IL-4 and shares some of its biologic functions. We investigated the effects of IL-13 on normal human B-cell precursors (BCP) and their malignant counterparts in B-lineage acute lymphoblastic leukemia (BCP-ALL). IL-13 inhibited growth of CD19+ slg- normal BCP cultured in the presence or absence of bone marrow accessory stromal cells and IL-7. In addition, IL-13 inhibited proliferation of blasts isolated from leukemic patients and cells from established BCP-ALL lines. Differences were observed in a number of cases with respect to growth inhibition in response to IL-13 and IL-4. These results suggest heterogeneity in the expression of IL-13 and IL-4 receptors in B-cell ontogeny. Growth-inhibition by IL-13 could be reverted by anti-IL-4 receptor antibody, indicating that the IL-13 and IL-4 binding chains can be closely associated on BCP. We further showed that the inhibitory effect of IL-13 results from decreased cell-cycle activity. Finally, whereas IL-13 induced CD23 expression on BCP-ALL cells, it did not promote differentiation into slg+ B lymphocytes.

L6 ANSWER 19 OF 21 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 95045516 MEDLINE
DOCUMENT NUMBER: 95045516
TITLE: Design of human interleukin-4 antagonists inhibiting interleukin-4-dependent and interleukin-13-dependent responses in T-cells and B-cells with high efficiency.
AUTHOR: Tony H P; Shen B J; Reusch P; Sebald W
CORPORATE SOURCE: Medizinische Poliklinik, Universitat, Wurzburg, Germany.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, **(1994 Oct 15)** 225 (2) 659-65.
Journal code: EMZ. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
ENTRY MONTH: 199502
AB Human interleukin-4 possesses two distinct sites for receptor activation. A signalling site, comprising residues near the C-terminus on helix D, determines the efficacy of interleukin-4 signal transduction without affecting the binding to the interleukin-4 receptor alpha subunit. A

complete antagonist and a series of low-efficacy agonist variants of human interleukin-4 could be generated by introducing combinations of two or three negatively charged aspartic acid residues in this site at positions 121, 124, and 125. One of the double variants, designated [R121D,Y124D]interleukin-4, with replacements of both Arg121 and Tyr124 by aspartic acid residues was completely inactive in all analysed cellular responses. The loss of efficacy in [R121D,Y124D]interleukin-4 is estimated to be larger than 2000-fold. Variant [R121D,Y124D]interleukin-4 was also a perfect antagonist for inhibition of interleukin-13-dependent responses in B-cells and the TF-1 cell line with a Ki value of approximately 100 pM. In addition, inhibition of both interleukin-4-induced and interleukin-13-induced responses could be obtained by monoclonal antibody X2/45 raised against interleukin-4Rex, the extracellular domain of the interleukin-4 receptor alpha subunit. These results indicate that efficient interleukin-4 antagonists can be designed on the basis of a sequential two-step activation model. In addition, the experiments indicate the functional participation of the interleukin-4 receptor alpha subunit in the **interleukin-13 receptor** system.

L6 ANSWER 20 OF 21 MEDLINE
ACCESSION NUMBER: 93327755 MEDLINE
DOCUMENT NUMBER: 93327755
TITLE: Receptors for interleukin-13 and interleukin-4 are complex and share a novel component that functions in signal transduction.
AUTHOR: Zurawski S M; Vega F Jr; Huyghe B; Zurawski G
CORPORATE SOURCE: Department of Molecular Biology, DNAX Research Institute for Molecular and Cellular Biology, Palo Alto, CA 94304-1104.
SOURCE: EMBO JOURNAL, **(1993 Jul)** 12 (7) 2663-70.
Journal code: EMB. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
AB Interleukin-4 (IL-4) and interleukin-13 (IL-13) are two cytokines that are secreted by activated T cells and have similar effects on monocytes and B cells. We describe a mutant form of human interleukin-4 (hIL-4) that competitively antagonizes both hIL-4 and human interleukin-13 (hIL-13). The amino acid sequences of IL-4 and IL-13 are approximately 30% homologous and circular dichroism (CD) spectroscopy shows that both proteins have a highly alpha-helical structure. IL-13 competitively inhibited binding of hIL-4 to functional human IL-4 receptors (called hIL-4R) expressed on a cell line which responds to both hIL-4 and IL-13. Binding of hIL-4 to an hIL-4 responsive cell line that does not respond to IL-13, and binding of hIL-4 to cloned IL-4R ligand binding protein expressed on heterologous cells, were not inhibited by IL-13. hIL-4 bound with approximately 100-fold lower affinity to the IL-4R ligand binding protein than to functional IL-4R. The mutant hIL-4 antagonist protein bound to both IL-4R types with the lower affinity. The above results demonstrate that IL-4 and IL-13 share a receptor component that is important for signal transduction. In addition, our data establish that IL-4R is a complex of at least two components one of which is a novel affinity converting subunit that is critical for cellular signal transduction.

L6 ANSWER 21 OF 21 MEDLINE
ACCESSION NUMBER: 94065589 MEDLINE
DOCUMENT NUMBER: 94[redacted]589
TITLE: An interleukin 4 (IL-4) mutant protein inhibits both IL-4 or IL-13-induced human immunoglobulin G4 (IgG4) and IgE synthesis and B cell proliferation: support for a common component shared by IL-4 and IL-13 receptors.
AUTHOR: Aversa G; Punnonen J; Cocks B G; de Waal Malefyt R; Vega F Jr; Zurawski S M; Zurawski G; de Vries J E
CORPORATE SOURCE: Human Immunology Department, DNAX Research Institute, Palo Alto, California 94304-1104.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, **(1993 Dec 1)** 178 (6) 2213-8.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199403

AB Interleukin 4 (IL-4) and IL-13 share many biological functions. Both cytokines promote growth of activated human B cells and induce naive human surface immunoglobulin D+ (sIgD+) B cells to produce IgG4 and IgE. Here we show that a mutant form of human IL-4, in which the tyrosine residue at position 124 is replaced by aspartic acid (hIL-4.Y124D), specifically blocks IL-4 and IL-13-induced proliferation of B cells costimulated by anti-CD40 mAbs in a dose-dependent fashion. A mouse mutant IL-4 protein (mIL-4.Y119D), which antagonizes the biological activity of mouse IL-4, was ineffective. In addition, hIL-4.Y124D, at concentrations of up to 40 nM, did not affect IL-2-induced B cell proliferation. hIL-4.Y124D did not have detectable agonistic activity in these B cell proliferation assays. Interestingly, hIL-4.Y124D also strongly inhibited both IL-4 or IL-13-induced IgG4 and IgE synthesis in cultures of peripheral blood mononuclear cells, or highly purified sIgD+ B cells cultured in the presence of anti-CD40 mAbs. IL-4 and IL-13-induced IgE responses were inhibited > 95% at a approximately 50- or approximately 20-fold excess of hIL-4.Y124D, respectively, despite the fact that the IL-4 mutant protein had a weak agonistic activity. This agonistic activity was 1.6 +/- 1.9% (n = 4) of the maximal IgE responses induced by saturating concentrations of IL-4. Taken together, these data indicate that there are commonalities between the IL-4 and IL-13 receptor. In addition, since hIL-4.Y124D inhibited both IL-4 and IL-13-induced IgE synthesis, it is likely that antagonistic mutant IL-4 proteins may have potential clinical use in the treatment of IgE-mediated allergic diseases.